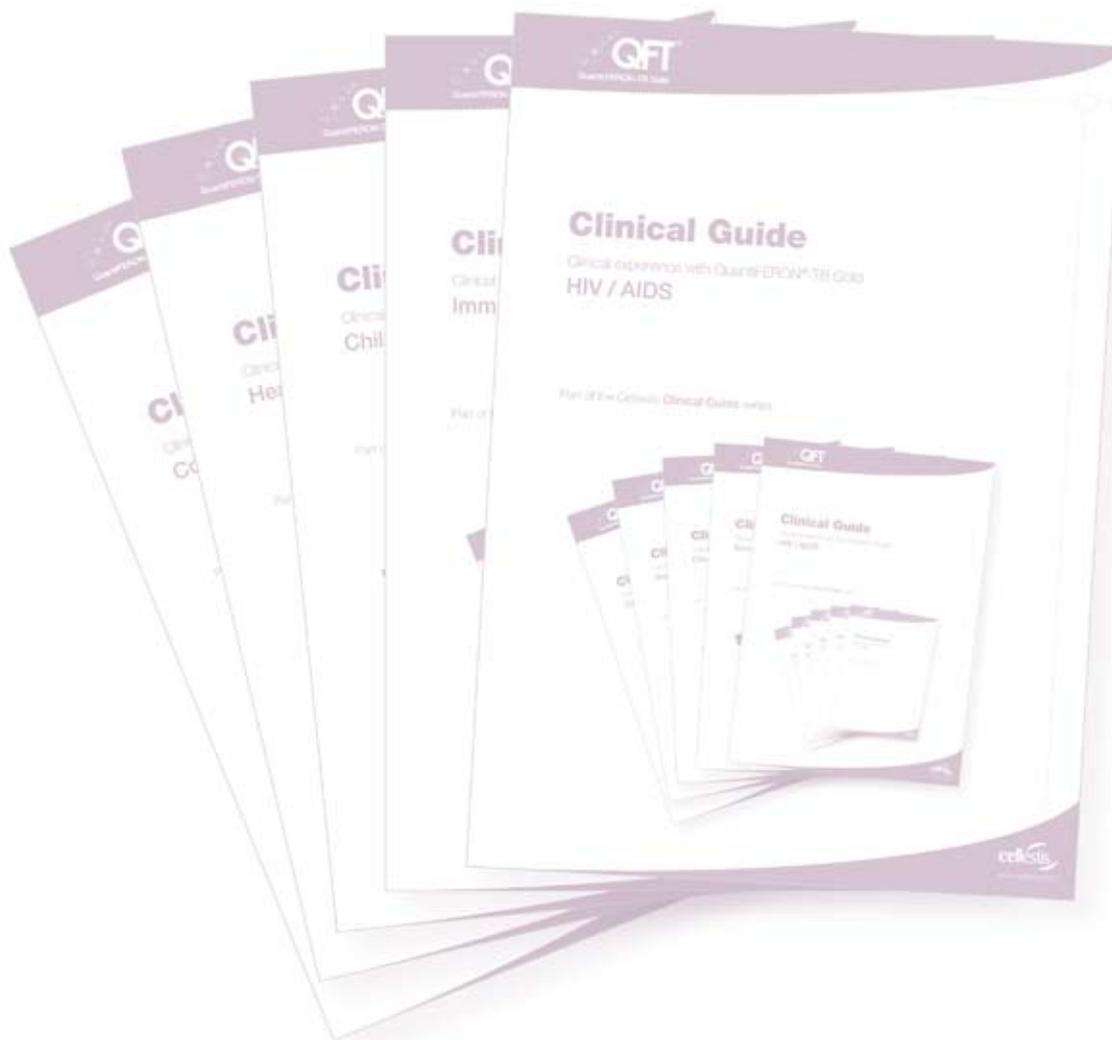


# Literature Overview

Experience with QuantiferON®-TB Gold

## Health Economics



This literature overview is intended to provide healthcare professionals with a summary of current health economic assessments and reviews of using QuantiFERON®-TB Gold (QFT™) in different situations and geographies.

## Summary of published health economic assessments

### USA/Canada economic assessments

De Perio MA, Tsevat J, Roselle GA, Kralovic SM, Eckman MH. The cost-effectiveness of Interferon-γ release assays vs. Tuberculin skin tests for detecting latent tuberculosis infection in healthcare workers. *Presented at Infectious Diseases Society of America, Oct 2007.*

“In this assessment a Markov model was used to compare the cost effectiveness of 3 strategies (QuantiFERON-TB Gold In-Tube, QuantiFERON-TB Gold and Tuberculin Skin Test (TST)) for detecting LTBI in new health care workers (HCW) with or without prior BCG vaccination.”

It showed that for non-BCG vaccinated HCW, the incremental cost effectiveness of QuantiFERON-TB Gold, compared with QuantiFERON-TB Gold In-Tube was \$US14,092/QALY. For BCG vaccinated HCWs, the incremental cost-effectiveness of QuantiFERON-TB Gold was \$US 103,020/QALY. Sensitivity analyses show that if the sensitivity of QuantiFERON-TB Gold In-Tube exceeds that of QuantiFERON-TB Gold (which it does), QuantiFERON-TB Gold In-Tube is the most effective and least costly strategy. The direct costs of each strategy are outlined below.

| Testing strategy            | Cost (non-BCG vaccinated cohort) | Cost (BCG vaccinated cohort) |
|-----------------------------|----------------------------------|------------------------------|
| QuantiFERON-TB Gold In-Tube | \$US240.57                       | \$US 162.47                  |
| QuantiFERON-TB Gold         | \$US241.73                       | \$US 166.39                  |
| TST                         | \$US256.82                       | \$US263.66                   |

Dewan PK, Grinsdale J, Liska S, Wong E, Fallstad R, Kawamura LM. Feasibility, acceptability, and cost of tuberculosis testing by whole-blood interferon-gamma assay. *BMC Infect Dis 2006; 6:47.*

This study evaluated the feasibility and costs of QuantiFERON-TB\* use in six community clinics (in San Francisco) serving homeless, immigrant and injection-drug using populations over a period of one and a half years. Of the 4,143 people tested, positive or negative QFT results were available for 3,829 (92%) people, while only 89 (2%) were QFT indeterminate. The total cost of running QFT was \$US 33.67 per patient tested, which included phlebotomy, laboratory, and personnel costs.

\*Study used QuantiFERON-TB, which has lower sensitivity and specificity than the current generation test (QuantiFERON-TB Gold In-Tube).

Oxlade O, Schwartzman K, Menzies D. Interferon-gamma release assays and TB screening in high-income countries: a cost-effectiveness analysis. *Int J Tuberc Lung Dis 2007; 11:16-26.*

The researchers used a Markov model to compare the expected TB cases and costs of various screening methods among immigrants to Canada and TB contacts over a period of 20 years. Sequential screening with TST then QFT was more cost-effective than QFT alone in all scenarios and more cost-effective than TST alone in selected subgroups. In both immigrants and TB contacts who had received BCG vaccination after infancy, QFT was more cost-effective than TST, because of reduced TST specificity.

## German economic assessments

Diel R, Nienhaus A, Loddenkemper R. Cost-effectiveness of interferon gamma release assay screening for latent tuberculosis infection treatment in Germany. *Chest* 2007; 5:1424-34.

A Markov model was used to assess the health and economic outcomes of isoniazid treatment of 20 year old TB contacts using two different TST cut-offs (5 mm and 10 mm), QFT alone and QFT as a confirmatory test for TST results. The number treated to prevent one TB case was 22 for the two QFT based procedures, 40 for the TST at a cut-off of 10 mm, and 96 for the TST at a cut-off of 5 mm “which may appear to be a striking argument from an ethical point of view” for using only QFT.

This analysis showed that the two TST-based strategies “when performed alone, in each case [was] more costly and less effective than the QFT-G [Quantiferon®-TB Gold in-Tube] assay, the higher cost of implementation of which was outweighed by the averted cost of unnecessarily treating contacts who otherwise would have been wrongly classified as LTBI cases.”

Of the four strategies, QFT following the TST screening of close-contacts at a cut-off of 5 mm was the most cost-effective option, followed by the QFT alone strategy. However the cost of combining the two tests was “only marginally lower than the total cost of the program based on QFT-G assay alone per 1000 close-contacts by approximately \$ 1,397 (0.61%).”

Diel R, Nienhaus A, Lange C, Schaberg T. Cost optimization of screening for latent tuberculosis in close contacts. *Eur Respir J* 2006; 28:35-44.

In a German cost-minimisation analysis, the costs of investigating a cohort of adult tuberculosis (TB) contacts over a period of 2 years was calculated. In this assessment the total cost of simply administering the TST was € 19.24 per person (includes tuberculin material costs, as well as TST administration and reading costs) while the total cost of performing QFT was € 47.68 per person (includes blood sampling, sample transport and all laboratory material and labour costs). These costs DO NOT include follow up costs for those testing positive by either test. Such follow-up comprised three chest X-rays at a cost of € 74.3 per X-ray—which includes all labour and material costs of performing a chest X-ray. This analysis showed that:

- When TST was used alone the average costs for every contact followed amounted to € 91.
- If instead of TST, QFT alone was performed, the cost per contact was reduced by 33% to € 61.
- If both test were combined (validation of a positive TST by QFT) the costs were reduced by 43% to € 52.

A two step approach proved to be marginally cost effective compared to only using QFT. However this sacrifices the operational ease of only using QFT, but also has the risk of missing individuals (eg. those with immunosuppression) with false negative TST results. As a result the authors do state that “the TST/QFT-G two step strategy should be reassessed in the presence of such specific epidemiological conditions.”

## UK economic assessments

UK National Institute for Health and Clinical Excellence (NICE). Tuberculosis clinical guideline—full guideline, second consultation.\*

NICE considered the cost-effectiveness of 4 different strategies—no test (inform and advise), TST alone, interferon gamma release assay (IGRA) alone and IGRA testing for individuals with a positive TST—for diagnosing latent tuberculosis infection (LTBI). The assessment showed that:

- At all prevalence levels, an IGRA-only strategy was cheaper than a TST-only strategy.
- Overall, the two-stage TST/IGRA strategy was most cost effective, however the impact of false negative results or logistical issues involved with two step testing was not considered in the assessment.
- One step IGRA testing can be used in individuals “in whom tuberculin skin testing may not be reliable” such as those with immune suppressing diseases (including HIV) or on immune suppressive treatment (e.g. corticosteroids), Hodgkin’s disease, infectious mononucleosis and viral infections in general (including those of the upper respiratory tract).
- The NICE assessment showed that above a prevalence level of 40%, one step testing (that is a single IGRA test) is the most cost effective option.

NICE guidelines state that “Interferon-gamma tests showed little evidence of being affected by prior BCG vaccination, and showed stronger correlation with exposure categories than did TST...The specificity of interferon-gamma tests seemed better, and there was less potential for false positive results.”

Despite this being meant as an analysis of IGRAs in general, it appears the QFT was exclusively used, as an IGRA cost of £16 was used—which reflects QFT rather than Elispot pricing.

\*Accessed on 14 January 2007 at <http://www.nice.org.uk/guidance/index.sp?action=download&o=30007>

## Japan economic assessments

Mori T, Harada N. Cost-effectiveness analysis of QuantiFERON-TB 2nd generation used for detection of tuberculosis infection in contact investigations. *Kekkaku* 2005; 80:675-86 [Article in Japanese].

A cost-effectiveness analysis of QFT in a TB contact investigation in Japan. A model was built assuming that a group of young people was exposed to an infection source with different degrees of intensity. The strategies for investigating this group included using QFT to test subjects with erythema size exceeding 30 mm, 20 mm and 10 mm, as compared with the strategy of only using TST or QFT. The analysis confirmed that the additional use of QFT would greatly reduce the number of indications for chemoprophylaxis of uninfected cases and that the use of QFT is cost effective.

## Clinical Advantages

### QFT clinical advantages that provide economic benefits for TB infection control programs—

- Single visit.
- High sensitivity (up to 93%) and specificity (>99%) for detecting active TB.<sup>(1)</sup>  
*Avoids false positives due to BCG vaccination<sup>(2)</sup> and most environmental non-tuberculous mycobacteria<sup>(3)</sup>*
- Unlike the TST is not subject to errors in test placement or reading.
- Reduction in personnel cost—which is the major cost component of a TST program.  
*TST reagents represent less than 1.5% of the total cost of TST screening programs.<sup>(4)</sup>*
- Reduction in additional costs—such as chest X-rays—associated with investigating false positive cases.<sup>(5)</sup>
- Avoids Boosting.<sup>(6)</sup>  
*Eliminates need for 2-step testing.*

**“In situations with serial testing for *M. tuberculosis* infection, initial two-step testing—which is necessary with the TST—is unnecessary with QFT-G [QuantiFERON-TB Gold] and is not recommended”.<sup>(7)</sup>**

## References

1. Harada N, Higuchi K, Yoshiyama T, Kawabe Y, Fujita A, Sasaki Y, Horiba M, Mitarai S, Yonemaru M, Ogata H, Ariga H, Kurashima A, Wada A, Takamori M, Yamagishi F, Suzuki K, Mori T, Ishikawa N. Comparison of the sensitivity and specificity of two whole blood interferon-gamma assays for *M. tuberculosis* infection. *J Infect* 2008; 56:348–53.
2. Mori T, Sakatani M, Yamagishi F, Takashima T, Kawabe Y, Nagao K, Shigeto E, Harada N, Mitarai S, Okada M, Suzuki K, Inoue Y, Tsuyuguchi K, Sasaki Y, Mazurek GH, Tsuyuguchi I. Specific detection of tuberculosis infection: an interferon-gamma-based assay using new antigens. *Am J Respir Crit Care Med* 2004; 170:59–64.
3. Anderson P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of TB. *Lancet* 2000; 356:1099–104.
4. Lambert L, Rajbhandary S, Quails N, Budnick L, Catanzaro A, Cook S, Daniels-Cuevas L, Garber E, Reves R. Costs of Implementing and Maintaining a Tuberculin Skin Test Program in Hospitals and Health Departments. *Infect Control Hosp Epidemiol* 2003; 24:814–20.
5. Nienhaus A, Schablon A, Le Bâcle C, Siano B, Diel R. Evaluation of the interferon-release assay in healthcare workers. *Int Arch Occup Environ Health* 2008; 81:295–300.
6. Leyten EM, Prins C, Bossink AW, Thijsen S, Ottenhoff TH, van Dissel JT, Arend SM. Effect of tuberculin skin testing on a Mycobacterium tuberculosis-specific IFN- $\gamma$  assay. *Eur Respir J* 2007; 29:1212–6.
7. Centers for Disease Control. *MMWR Dec 16 2005, Vol. 54, No. RR-15.*

For more information, please contact the Cellestis office nearest you or visit [www.cellestis.com](http://www.cellestis.com).

**North America / South America**  
Cellestis Inc.  
Email: [customer.service@cellestis.com](mailto:customer.service@cellestis.com)  
Fax: +1 661 775 7479  
Tel: +1 661 775 7480 (outside USA)  
Toll free: 800 519 4627 (USA only)

**Europe / Middle East / Africa**  
Cellestis GmbH  
Email: [europa@cellestis.com](mailto:europa@cellestis.com)  
Fax: +49 6151 428 59 110  
Tel: +49 6151 428 59 0

**Asia / Oceania**  
Cellestis International  
Email: [quantiferon@cellestis.com](mailto:quantiferon@cellestis.com)  
Fax: +61 3 9571 3544  
Tel: +61 3 9571 3500